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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,481	01/20/2004	Nozer M. Mehta	P/546-280	2921

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EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	**PAPER NUMBER**
1654	

MAIL DATE	DELIVERY MODE
11/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/761,481	MEHTA ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63 and 65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-60,62,63 and 65* is/are rejected.

7)☒ Claim(s) *61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on May 10, 2007 has been entered.

2. Applicant is advised that should claim 45 be found allowable, claim 62 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 45 and 62 are identical in scope.

3. The effective filing date of instant claims 1-63 is January 21, 2003, the filing date of provisional application 60/441,856. Instant claims 1-63 are deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of the provisional application because the provisional application, under the test of 35 U.S.C. 112, first paragraph, discloses the claimed subject matter.

The effective filing date of instant claim 65 is January 20, 2004, the filing date of the instant application. Instant claim 65 is not deemed to be entitled under 35 U.S.C. 119(e) to the benefit of the filing date of provisional application 60/441,856 because the provisional application, under the test of 35 U.S.C. 112, first paragraph, does not disclose general pharmaceutical compositions for oral delivery in which the PTH 1-34-OH are not amidated.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-8, 12-47, 49-51, 54-60, 62, 63, and 65 are rejected under 35 U.S.C. 103(a) as being obvious over Stern et al (U.S. Patent No. 6,086,918) in view of Habener (U.S. Patent No. 5,120,712), Balschmidt et al (U.S. Patent No. 5,157,021), Barbier et al (U.S. Patent No. 6,110,892), the European Patent Application 878,201, or Neiss et al (U.S. Patent No. 4,804,742). Stern et al teach oral administration of peptides such as insulin, salmon calcitonin, parathyroid hormone, and lhrf using a carrier comprising a pH-lowering agent, an absorption enhancer, a non-physiologically active protein, a gelatin capsule, and an enteric coating. See, e.g., column 6, line 1 - column 12, line 10, and claims 1-55. Stern et al do not teach peptides which are amidated GLP-1 analogs, amidated insulin analogs, or amidated PTH analogs. Habener teaches GLP-1 analogs which are amidated. See, e.g., claims 1 and 4. Balschmidt et al teach insulin in which the carboxylic acid groups present in the sidechains at residues A4, A17, B13, and B21 are amidated in order to achieve a long-lasting protracted acting insulin analog. See, e.g., column 2, lines 5-8 and 49-53. Barbier et al teach the human parathyroid hormone derivatives hPTH(1-34)-OH and hPTH(1-31)NH_2. See, e.g., column 2, lines 26-44. The European Patent Application '201 teaches the human parathyroid hormone derivative hPTH(1-34)NH_2. See, e.g., column 3, lines 31-36. Neiss et al teach salmon calcitonin amidated at locations which are not naturally amidated and which have extended duration of activity. See, e.g., column 1, lines 42-44, and claims 1 and 2. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al in the oral administration

compositions of Stern et al because the oral administration compositions of Stern et al have general applicability to any peptide and because it would be desirable to be able to administer orally the peptides of Habener, Balschmidt et al, Barbier, the European Patent Application '201, and Neiss et al because oral administration is easier for the patient. Applicants' claims would have been prima facie obvious at the time the invention was made because applying Stern et al's known and generally applicable technique, i.e. of combining peptides with a pH-lowering agent, an absorption enhancer, a non-physiologically active protein, a gelatin capsule, and an enteric coating so that the peptides can be administered orally, to the known and specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al, with only the expected result that the known and specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al can be administered orally, is prima facie obvious. See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (S. Ct. 2007). With respect to instant claim 5, process limitations do not impart novelty and unobviousness to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

6. Claims 5 and 48 are rejected under 35 U.S.C. 103(a) as being obvious over Stern et al (U.S. Patent No. 6,086,918) in view of Habener (U.S. Patent No. 5,120,712), Barbier et al (U.S. Patent No. 6,110,892), the European Patent Application 878,201, or Neiss et al (U.S. Patent No. 4,804,742) as applied against claims 1-8, 12-47, 49-51, 54-60, 62, 63, and 65 above, and further in view of Stern et al (U.S. Patent No. 5,912,014). Habener, Barbier et al, the European Patent Application '201, and Neiss et al teach known and specific peptides which are amidated at their C-termini, but do not teach synthesizing these peptides by forming glycine-extended precursors

and then converting the glycine residue to a C-terminal amide group. Stern et al '014 teaches salmon calcitonin made with a C-terminal glycine extension which is enzymatically converted to an amide group. See, e.g., column 5, lines 12-23. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the known and specific peptides of Habener, Barbier et al, the European Patent Application '201, or Neiss et al for use in the oral administration compositions of Stern et al '918 by synthesizing the peptides as glycine-extended precursors and then converting the glycine residue to a C-terminal amide group, because Stern et al '014 teach that this is a known reaction technique for forming a C-terminally amidated peptide, and because the particular method of synthesizing a peptide would not have been expected to affect the in vivo activity of the peptide.

7. Claims 1-47, 49-60, 62, 63, and 65 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 02/043767 in view of Habener (U.S. Patent No. 5,120,712), Balschmidt et al (U.S. Patent No. 5,157,021), Barbier et al (U.S. Patent No. 6,110,892), the European Patent Application 878,201, or Neiss et al (U.S. Patent No. 4,804,742). The WO Patent Application '767 teaches oral administration of peptides such as insulin, salmon calcitonin, parathyroid hormone, lhrf, and GLP-1 linked to a membrane translocator using a carrier comprising a pH-lowering agent, a protease inhibitor, an absorption enhancer, a non-physiologically active peptide, a gelatin capsule, and an enteric coating. See, e.g., page 17, lines 13-22, page 18, lines 10-27, page 20, lines 11-29, and claims 1-57. [Note that the WO Patent Application '767 does not designate the US, and therefore is not available as prior art under 35 U.S.C. 102(e).] The WO Patent Application '767 does not teach peptides which are amidated GLP-1 analogs, amidated insulin analogs, or amidated PTH analogs. Habener teaches GLP-1

analogs which are amidated. See, e.g., claims 1 and 4. Balschmidt et al teach insulin in which the carboxylic acid groups present in the sidechains at residues A4, A17, B13, and B21 are amidated in order to achieve a long-lasting protracted acting insulin analog. See, e.g., column 2, lines 5-8 and 49-53. Barbier et al teach the human parathyroid hormone derivatives hPTH(1-34)-OH and hPTH(1-31)NH_2. See, e.g., column 2, lines 26-44. The European Patent Application '201 teaches the human parathyroid hormone derivative hPTH(1-34)NH_2. See, e.g., column 3, lines 31-36. Neiss et al teach salmon calcitonin amidated at locations which are not naturally amidated and which have extended duration of activity. See, e.g., column 1, lines 42-44, and claims 1 and 2. It would have been obvious to one of ordinary skill in the art at the time Applicant's invention was made to use the specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al in the oral administration compositions of the WO Patent Application '767 because the oral administration compositions have general applicability to any peptide and because it would be desirable to be able to administer orally the peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, and Neiss et al because oral administration is easier for the patient. Applicants' claims would have been prima facie obvious at the time the invention was made because applying the WO Patent Application '767's known and generally applicable technique, i.e. of combining peptides with a pH-lowering agent, a protease inhibitor, an absorption enhancer, a non-physiologically active peptide, a gelatin capsule, and an enteric coating so that the peptides can be administered orally, to the known and specific peptides of Habener, Balschmidt et al, Barbier et al, the European Patent Application '201, or Neiss et al, with only the expected result that the known and specific peptides of Habener, Balschmidt et al, Barbier et

al, the European Patent Application '201, or Neiss et al can be administered orally, is prima facie obvious. See KSR International Co. v. Teleflex Inc., 82 USPQ2d 1385 (S. Ct. 2007). With respect to instant claim 5, process limitations do not impart novelty and unobviousness to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

8. Claims 5 and 48 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 02/043767 in view of Habener (U.S. Patent No. 5,120,712), Barbier et al (U.S. Patent No. 6,110,892), the European Patent Application 878,201, or Neiss et al (U.S. Patent No. 4,804,742) as applied against claims 1-47, 49-60, 62, 63, and 65 above, and further in view of Stern et al (U.S. Patent No. 5,912,014). Habener, Barbier et al, the European Patent Application '201, and Neiss et al teach known and specific peptides which are amidated at their C-termini, but do not teach synthesizing these peptides by forming glycine-extended precursors and then converting the glycine residue to a C-terminal amide group. Stern et al '014 teaches salmon calcitonin made with a C-terminal glycine extension which is enzymatically converted to an amide group. See, e.g., column 5, lines 12-23. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to form the known and specific peptides of Habener, Barbier et al, the European Patent Application '201, and Neiss et al for use in the oral administration compositions of the WO Patent Application '767 by synthesizing the peptides as glycine-extended precursors and then converting the glycine residue to a C-terminal amide group, because Stern et al '014 teaches that this is a known reaction technique for forming a C-terminally amidated peptide, and because the particular method of synthesizing a peptide would not have been expected to affect the in vivo activity of the peptide.

9. Claims 1, 6, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Balschmidt et al (U.S. Patent No. 5,157,021). Balschmidt et al teach pharmaceutical compositions comprising insulin in which the carboxylic acid groups present in the sidechains at residues A4, A17, B13, and B21 are amidated in order to achieve a long-lasting protracted acting insulin analog. See, e.g., column 2, lines 5-8 and 49-53; column 3, line 64 - column 4, line 3; and claims 1-16. Note that an intended use limitation, e.g., "orally delivered", does not impart patentability to product claims where the product is otherwise anticipated by the prior art. Because Balschmidt et al teach the only component specified in Applicants' claims, i.e. an active peptide amidated at a location that is not naturally amidated, inherently the composition of Balschmidt et al will provide enhanced bioavailability of the amidated peptide when it is orally delivered to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the pharmaceutical compositions of Balschmidt et al and Applicants' claimed compositions to shift the burden to Applicants to provide evidence that the claimed compositions are unobviously different than those of Balschmidt et al.

10. Claims 1, 4, 5, and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Habener (U.S. Patent No. 5,120,712). Habener teaches pharmaceutical compositions comprising GLP-1 analogs which are amidated at the C-terminus. See, e.g., column 4, lines 14-29, and claims 1, 4, 5, and 7. Note that an intended use limitation, e.g., "orally delivered", does not impart patentability to product claims where the product is otherwise anticipated by the prior art. Because Habener teaches the only component specified in Applicants' claims, i.e. an active peptide amidated at a location that is not naturally amidated, inherently the composition of Habener will provide enhanced bioavailability of the amidated peptide when it is orally delivered

to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the pharmaceutical compositions of Habener and Applicants' claimed compositions to shift the burden to Applicants to provide evidence that the claimed compositions are unobviously different than those of Habener. With respect to instant claim 5, process limitations do not impart novelty and unobviousness to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

11. Claims 1, 4, 5, 40, and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Barbier et al (U.S. Patent No. 6,110,892). Barbier et al teach pharmaceutical compositions comprising hPTH(1-31)NH_2. See, e.g., column 9, lines 25-46. Note that an intended use limitation, e.g., "orally delivered", does not impart patentability to product claims where the product is otherwise anticipated by the prior art. Because Barbier et al teach the only component specified in Applicants' claims, i.e. an active peptide amidated at a location that is not naturally amidated, inherently the composition of Barbier et al will provide enhanced bioavailability of the amidated peptide when it is orally delivered to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the pharmaceutical compositions of Barbier et al and Applicants' claimed compositions to shift the burden to Applicants to provide evidence that the claimed compositions are unobviously different than those of Barbier et al. With respect to instant claim 5, process limitations do not impart novelty and unobviousness to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

12. Claims 1, 4, 5, 40, 42, 45, 47, 58, 60, 62, and 63 are rejected under 35 U.S.C. 102(e) as being anticipated by Peri et al (U.S. Patent Application Publication 2004/0023882). Peri et al

teach pharmaceutical compositions comprising hPTH(1-34) amidated at its C-terminus, including hPTH(1-34)NH_2. The compositions can be administered orally. See, e.g., paragraph [0064] and claims 1-2. Because Peri et al teach the only component specified in Applicants' claims, i.e. an active peptide amidated at a location that is not naturally amidated, inherently the composition of Peri et al will provide enhanced bioavailability of the amidated peptide when it is orally delivered, e.g., as a result of enhanced intestinal absorption, to the same extent claimed by Applicants. Sufficient evidence of similarity is deemed to be present between the pharmaceutical compositions of Peri et al and Applicants' claimed compositions to shift the burden to Applicants to provide evidence that the claimed compositions are unobviously different than those of Peri et al. With respect to instant claim 5, process limitations do not impart novelty and unobviousness to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

The subject matter disclosed by Peri et al and relied upon in the rejection is also disclosed in the provisional application, 60/378,082, upon which Peri et al claim priority under 35 U.S.C. 119(e). See, e.g., page 10, line 22, and claims 1 and 2 of the provisional application. Accordingly, Peri et al is available as prior art against the instant claims under 35 U.S.C. 102(e).

13. Applicant's arguments filed May 10, 2007 have been fully considered but they are not persuasive.

The examiner maintains his position for the reasons set forth in the final Office action mailed November 13, 2006 and in the Advisory action mailed May 22, 2007.

14. Claim 61 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and

any intervening claims. The prior art does not teach or suggest orally administering lh-rh which is amidated at a location which is not naturally amidated. Note that the claim does not embrace the synthesis and oral administration of naturally-occurring lh-rh, which is naturally amidated at its C-terminus. Claim 61 requires the lh-rh to be amidated at a location other than its C-terminus.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

November 15, 2007